The population-level impact of bivalent HPV vaccination on closely related non-vaccine types

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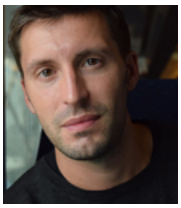

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Clinical trials of the both the bivalent and quadrivalent vaccine demonstrated a level of cross-protection against certain closely-related HPV types. However, a meta-analysis of clinical trial data from both vaccines suggested that the cross-protective efficacy against HPV31/33/45 infection and associated lesions was higher for the bivalent vaccine than the quadrivalent vaccine.[1] Since 2006, several countries have introduced national HPV vaccination programmes but relatively few countries introduced a national programme which exclusively adopted bivalent vaccine. Results of surveillance considering the population-level impact of HPV vaccination provide additional information to the clinical trials for several reasons. Firstly, in a real world setting, there may be some inequalities in who is being vaccinated, and secondly, that with high national vaccine coverage there will be a herd protection effect. Real-world post-vaccination surveillance studies have demonstrated clear reductions in HPV16/18 infections in many countries. As expected, the changes in non-vaccine types, which are often rarer, have taken longer to emerge than the changes in vaccine types. However, surveillance data from countries with a high-coverage vaccination programme using the bivalent vaccine demonstrate substantial declines in some non-16/18 HPV types.

In Scotland, prevalence of HPV 31, 33 or 45 in those aged 20/21 attending for first cervical screening test declined from 14.2% in those born in 1988 (unvaccinated cohort) to 2.6% in those born in 1995 (Figure 1). All cross-protective types showed significant vaccine effectiveness in those vaccinated at age 12/13 (HPV type 31, 93.8%; HPV type 33, 79.1%; HPV type 45, 82.6%). Unvaccinated individuals born in 1995 had a reduced odds of HPV16/18 infection compared with those born in 1988 (adjusted odds ratio 0.13 [95% confidence interval (CI); 0.06–0.28]) and reduced odds of HPV types 31, 33, and 45 (odds ratio 0.45) indicative of herd protection in this cohort.[2] Recent post-vaccination surveillance data from young women attending for chlamydia screening in England has also demonstrated a decline in the prevalence of HPV31/33/45 infection from 9.4% in females born in 1996-1998 (prior to vaccine introduction) to 1.4% in those born in 1998 (Figure 1).[3] The estimated vaccine effectiveness against

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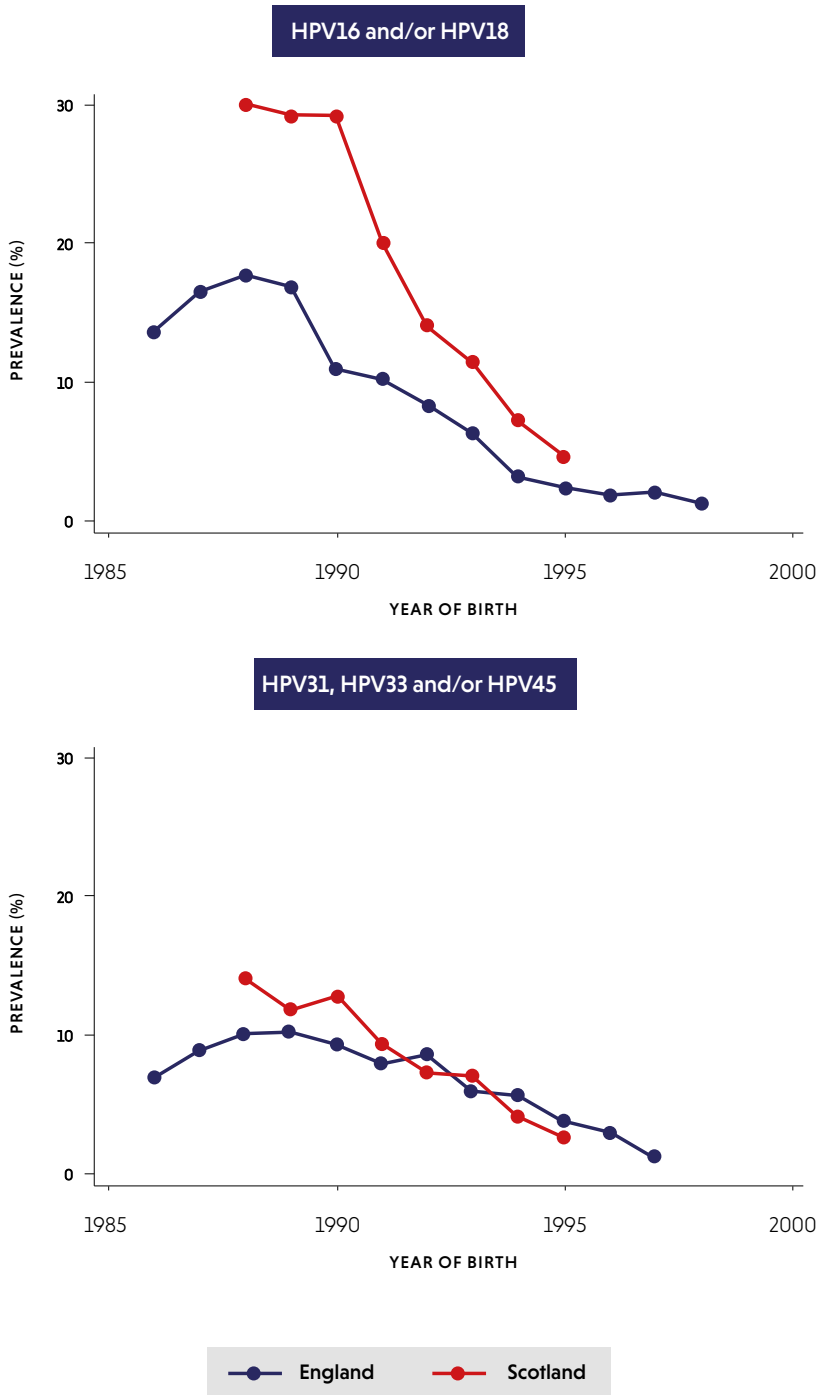
Figure 1

Prevalence of human papillomavirus (HPV) infection by year of birth and country



HPVIS/33/45 infection was 54.3% (95% CI; 8.6%-77.2%) for women who would have been offered vaccination at age 15 or younger.

Similar results of high vaccine-effectiveness have also been shown in other countries adopting the bivalent vaccine. For example, the results of a cohort study conducted in the Netherlands demonstrated a vaccine effectiveness against HPV 31, 33 and 45 persistent infections of 61.8% (95% CI; 16.7%-82.5%).[4] On first glance, the declines seen in these countries appear inconsistent with the moderate cross-protective efficacy from the clinical trials. However, the results are consistent with theoretical findings from mathematical models which have suggested that herd protection could have a relatively greater impact on declines in types with a lower basic reproductive number,[5] highlighting the importance of maintaining high vaccination coverage.

Mathematical models which have suggested that herd protection could have a relatively greater impact on declines in types with a lower basic reproductive number, highlighting the importance of maintaining high vaccination coverage

In summary, the declines in the prevalence of HPV31/33/45 infection in England and Scotland since the introduction of national HPV vaccination have been substantial. Together with HPV16/18, these types are associated with around 90% of cervical cancers in the UK. Elimination of these clinically relevant, high-risk HPV types in the United Kingdom is a real possibility and these data should inform assessments of the cost-effectiveness of introducing the nonavalent vaccine to national vaccination programmes. ■

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